



DEVELOPING ANTIBODIES AND VACCINES FOR CANCER

ANNUAL GENERAL MEETING

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LSE: SCLP.L

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USP: Targeting modified neo-antigens

Innovators in antibodies and vaccines

- Clinical stage company with two vaccine technology platforms and three vaccine products in clinical development
- Two antibody technology platforms with a deep preclinical pipeline
- Licensing deal with Genmab for one of our five mAbs – milestones of up to \$624m and single digit royalties

Specialist investor backing and strong financial position

- Supported by specialist biotech investors (Redmile Group, Vulpes)
- £82m raised to date, £33m in the last 2 years
- Cash runway to Q1 2024

Experienced team

- Experienced C-suite and board
- Expanding clinical development capability in-house to drive products forward
- Highly skilled team >50 employees headquartered in Oxford with research labs in Nottingham – have delivered four platforms creating multiple opportunities for proprietary projects and revenue-generating deals

Leveraging unique platforms to develop cutting edge products targeting modified neo-antigens



Four platforms delivering differentiated products for large unmet markets

ANTIBODIES

Targeting glycans preferentially expressed on tumours

GlyMab[®]

Anti-glycan mAb x 4

Targeting pancreatic, colorectal, small cell lung (SCLC) and ovarian cancer

Anti-glycan mAb x 1

Stimulating tumour infiltrating T cells

AvidiMab[®]

Antibody AvidiMab[®]

Broad potential for enhancing potency of any monoclonal antibody (mAb)

Vaccine AvidiMab[®]

Broad potential for enhancing potency of vaccines

VACCINES

Stimulating potent killer T cells

Moditope[®]

Modi-1

Citrullination

Phase 1/2 trial in triple negative breast (TNBC), ovarian, renal, head & neck cancer

Modi-2

Homocitrullination

Targeting breast, colorectal, non-small cell lung (NSCLC), prostate cancer

ImmunoBody[®]

SCIB1/iSCIB1+

Phase 2 trial in melanoma patients with immune checkpoint inhibitors
iSCIB1+ AvidiMab[®] modified multi-epitope vaccine

COVIDITY

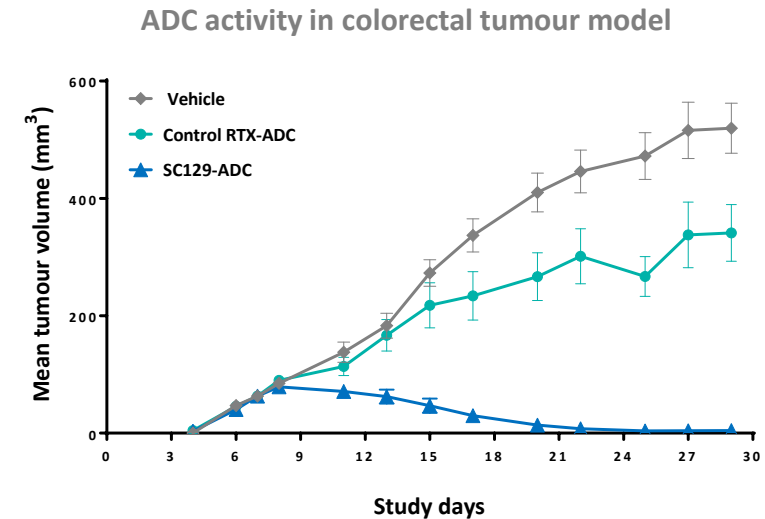
Adapted for COVID-19 trial

- ▶ SC129 mAb licensed to Genmab for antibody drug conjugates (ADC), T cell bispecifics (TCB) and radioimmunotherapy
- ▶ Upfront and milestone payments
- ▶ Milestones totalling up to \$624m, plus single digit royalties on sales
- ▶ Rights to SC129 for cell therapy products retained by Scancell



SC129 potential exemplified by internal and external preclinical studies

- ▶ SC129 binds strongly to pancreatic and colorectal tumours and has low expression on normal tissues
- ▶ Strong ADC activity demonstrated *in vivo*
- ▶ Direct and bystander killing demonstrated
- ▶ Activities confirmed during assessment by Genmab



Tivadar et al., Mol Cancer Ther., 2020 Mar;19(3):790-801

Key clinical outcomes with current funding



	Product	Indication	Research	Preclinical	Phase 1	Phase 2	Key outcomes
Vaccines	Modi-1	TNBC, ovarian, renal, head & neck	▶				Safety & immunological data H2 2022 Efficacy data 2023/24
	Modi-2	Multiple, solid tumours	▶				Enter the clinic H1 2024
	SCIB1/iSCIB1+	Late-stage melanoma	▶				Completion of SCOPE trial H2 2024
	COVIDITY	Covid-19	▶				Completion of the COVIDITY trial H1 2023
Antibodies	SC134 T cell bispecific	Small cell lung cancer	▶				Enter clinic H1 2024
	SC2811 Stimulatory mAb	Any solid tumour	▶				Lead candidate H1 2023
	GlyMab® Current & new	Multiple tumours	▶				Validation and deals on current and new targets
	AvidiMab®	Any mAb target	▶				Licensing deals

Clinically and commercially validated vaccine and antibody technology platforms with multiple value drivers



Four proprietary technology platforms delivering highly promising vaccine and antibody products: **clinically validated by three vaccines in Phase 1/2 and a further oncology vaccine to enter Phase 1 in 2024**

Vaccine portfolio has multiple near-term value inflection points, with **initial efficacy data** for Phase 2 oncology asset **expected in 2023** and a Phase 1 oncology asset with **early efficacy data expected in 2023**

Deep pre-clinical pipeline of anti-cancer antibodies leveraged from **two differentiated antibody platforms with broad commercial potential**

Deep scientific and strategic validation of monoclonal antibody portfolio and Glymab[®] platform through **\$624m¹ license agreement with leader in the field of antibody therapies for cancer, Genmab**

Antibody discovery engine to fuel the future pipeline to be developed either **internally or through co-development/licensing deals to drive further future value**

Experienced leadership and skilled scientific teams with a **track record of delivering multiple 'in-house' and clinically and commercially validated assets** which are backed by blue chip healthcare specialist investors

(1) Potential milestone payments of up to \$208 million for each product developed and commercialised with up to a maximum of \$624 million if Genmab develops and commercialises products across all defined modalities

Vaccines targeting stress induced post translational modifications

Vaccines: targeting modified neo-antigens to drive tumour-killing T cell responses



- ▶ Challenge with current cancer vaccines is that they stimulate low avidity T cells that fail to kill cancer cells
- ▶ Scancell's solutions are Moditope® which stimulates potent killer CD4 T cells against modified tumour neoepitopes and ImmunoBody® that stimulates potent (high avidity) killer CD8 responses in melanoma

Moditope® vaccines

- Significant increase in survival seen after vaccination in preclinical models

Modi-1

- Citrullinated peptides for TNBC, head and neck, ovarian, renal cancers
- Phase 1/2 study actively recruiting in UK

Modi-2

- Homocitrullinated peptides for multiple solid cancers
- Preclinical development underway

ImmunoBody® vaccines

- Cancer associated T cell epitopes engineered into a human antibody framework to make genetic antigen/antibody complex

SCIB1/iSCIB1+

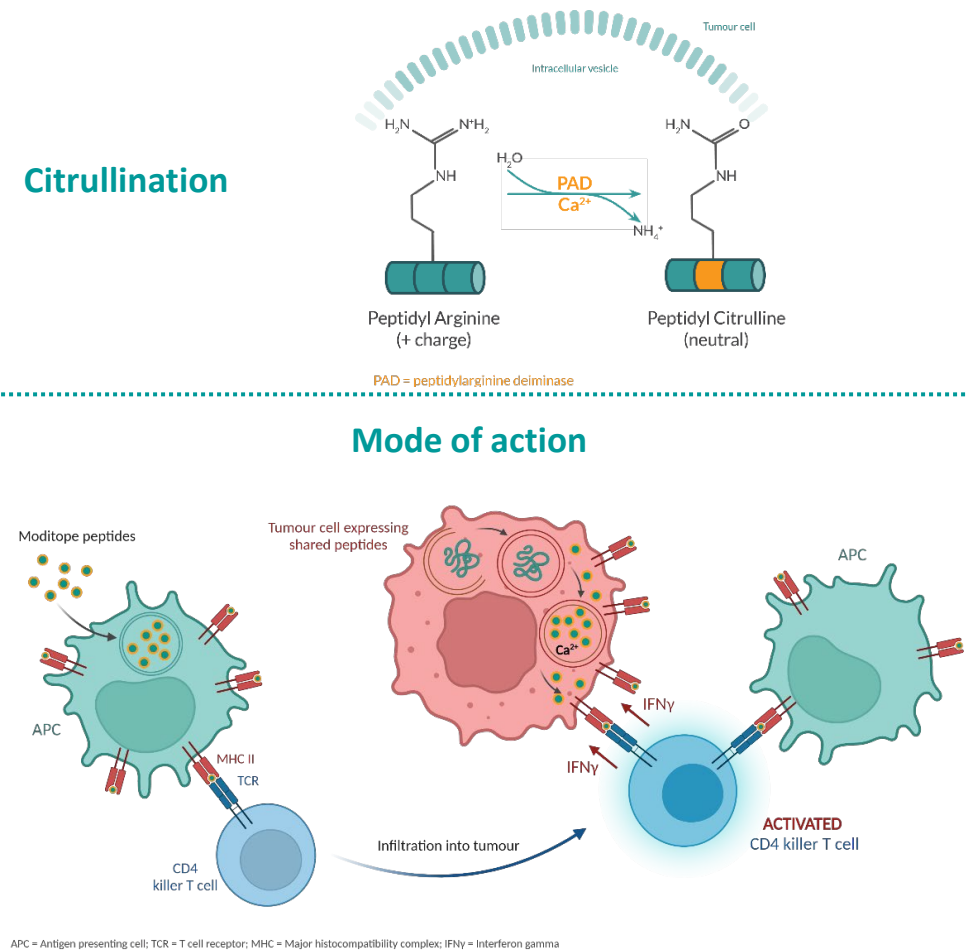
- SCIB1 Phase 2 clinical trial with immune checkpoint inhibitor ongoing in melanoma
- iSCIB1+ enhanced with AvidiMab® technology plus additional epitopes to broaden response and extend patent protection

COVIDITY

- Differentiated COVID-19 vaccine with needle-free delivery
- Phase 1 trial recruitment completed in South Africa

Vaccines targeting citrullination in cancer unique to Scancell (strong patent position)

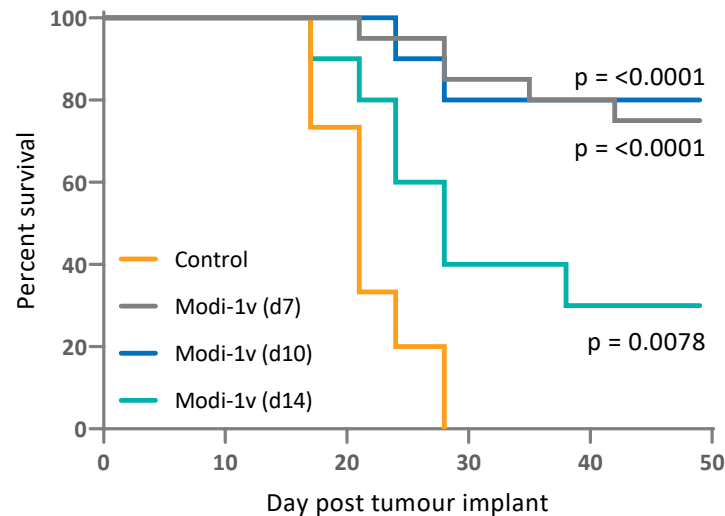
- ▶ The alteration of proteins due to enzymatic (PAD) conversion of arginine residues to citrulline
- ▶ Citrullination occurs as a result of autophagy induced in stressed cells, including cancer cells
- ▶ Citrullination protects from proteolytic cleavage and creates neo-epitopes
- ▶ Inflammation induces MHC class II expression and presentation of the citrullinated epitopes
- ▶ **Modi-1** product consists of:
 - ▶ Two citrullinated vimentin peptides
 - ▶ One citrullinated enolase peptide
 - ▶ Conjugated to Amplivant® adjuvant to boost immune response



Modi-1 vaccine is effective against advanced tumours

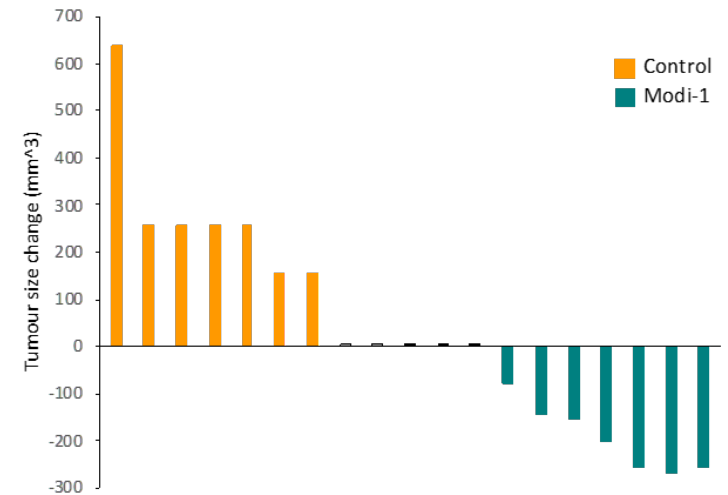
- ▶ B16cDR4 tumours established in HLA-DR4 transgenic mice (d1)
- ▶ Modi-1v (two vimentin peptides) plus adjuvant administered on d7, d10 or d14
- ▶ 30-80% of animals treated survived
- ▶ Survival in treated groups statistically significant

A single dose of Modi-1 results in significant survival response even against d14 tumours

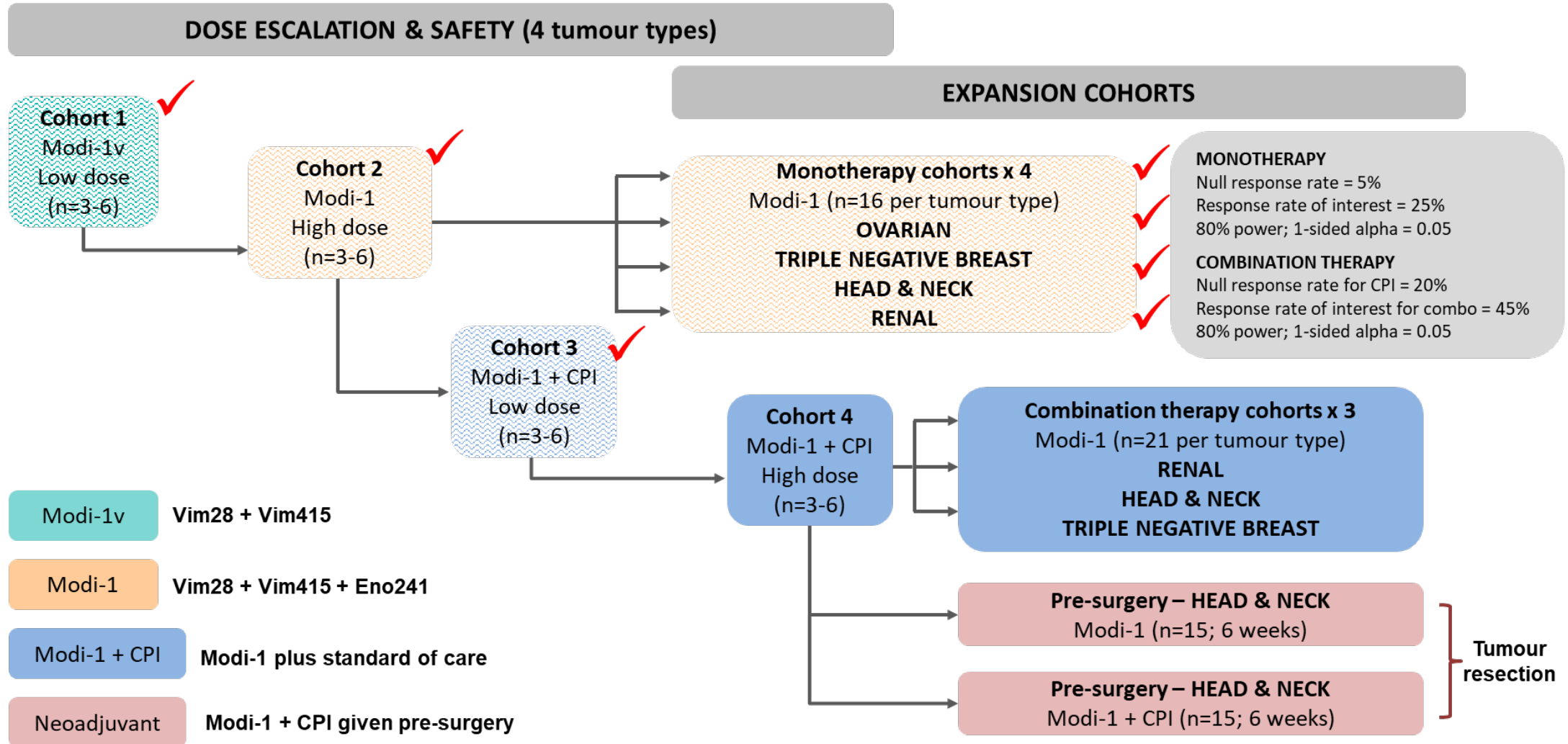


- ▶ B16iDP4 tumours established in DP4 transgenic mice (d1)
- ▶ Modi-1 peptides plus adjuvant administered when tumours reach more than 5 x 5 mm in size
- ▶ Tumour regression seen within 4 days of Modi-1 vaccination
- ▶ Correlates with rapid & potent immune responses

Modi-1 causes regression of established tumours within 4 days of immunisation



ModiFY Phase 1/2 trial actively recruiting patients in four tumour indications in the UK

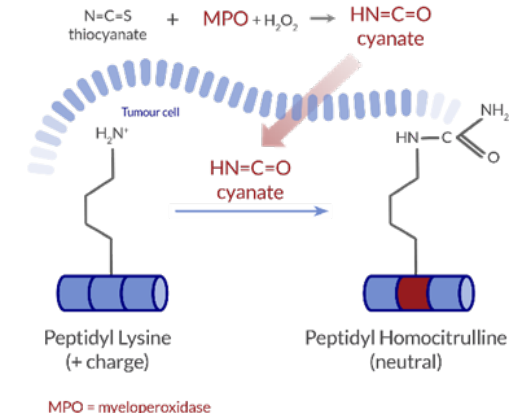


Moditope® targeting stress-induced homocitrullinated modified neo-antigens-Modi-2

Vaccines targeting homocitrullination in cancer unique to Scancell (strong patent position)

Homocitrullination

- ▶ Alteration of proteins via carbamylation which converts lysine residues into homocitrulline
- ▶ Carbamylation is mediated by myeloperoxidase which is produced by immune cells, including myeloid-derived suppressor cells found in the tumour microenvironment
- ▶ Homocitrullination results in a change in charge, ultimately generating unique T cell epitopes
- ▶ Modi-2 targeting breast, colorectal, non-small cell lung and prostate cancer



Modi-2

- ▶ Four homocitrullinated peptides from:
 - ▶ Aldolase A
 - ▶ Immunoglobulin binding protein (BiP)
 - ▶ Cytokeratin 8
 - ▶ Vimentin

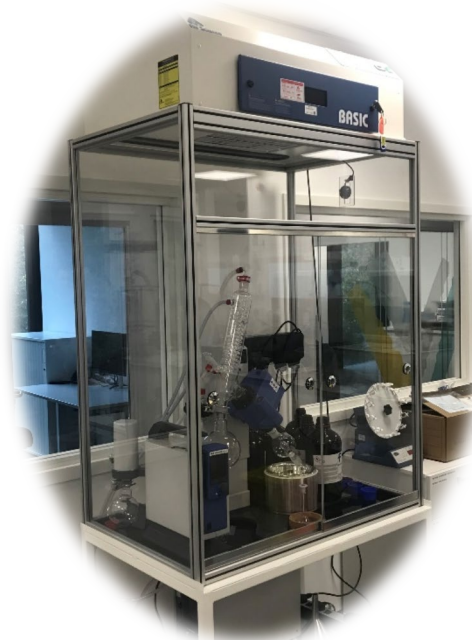
Modi-2

Formulation Development

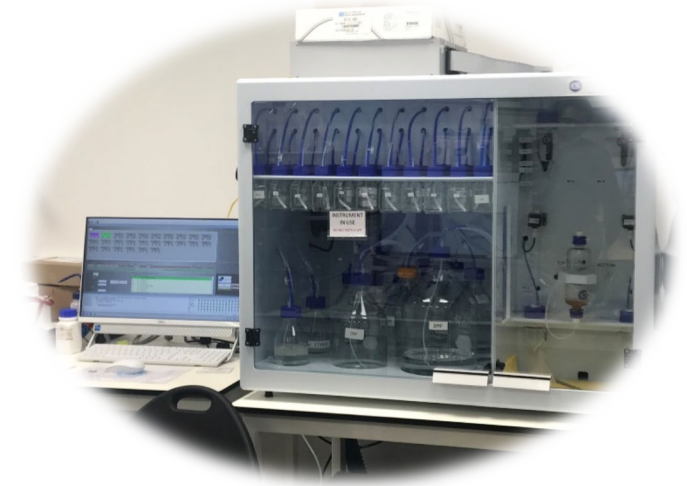
- ▶ Outsourcing of all drug manufacturing process development is time-limiting and expensive
 - ▶ Contract negotiations time-consuming
 - ▶ Slot availability for small-scale and large-scale batches restrictive
 - ▶ Lack of flexibility particularly for challenging products
 - ▶ Potential to reduce timelines and costs



HPLC – peptide purification; DNA analysis



Rotary evaporator – solvent removal

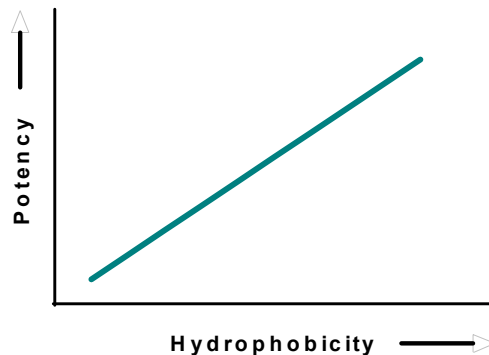


Peptide synthesizer

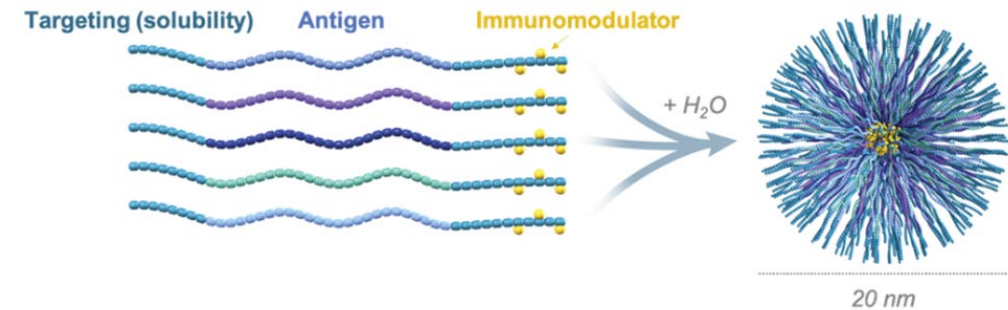
SNAPvax™ technology licensed from Vaccitech plc

Challenges

- ▶ Strong bias toward hydrophobic amino acids at T-cell receptor contact residues within immunogenic epitopes (Chowell et al., 2015)
- ▶ Hydrophobic peptides have challenging synthetic properties



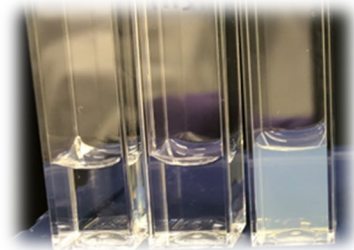
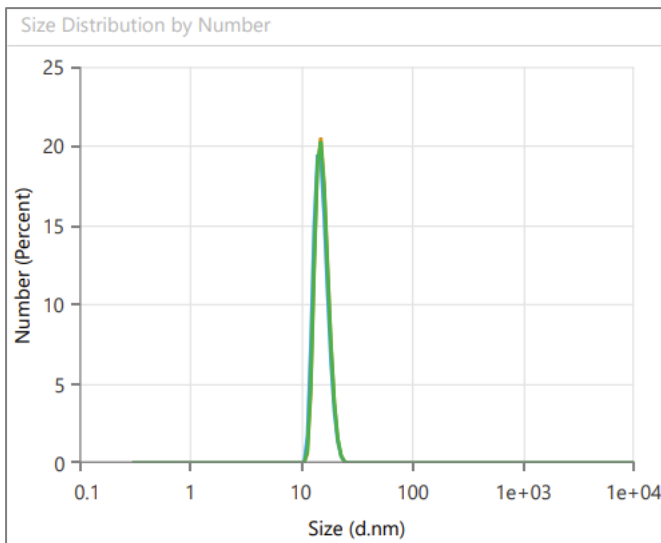
Nanoparticle formation



- ▶ Four homocitrullinated peptides
 - ▶ Each individual peptide conjugate synthesized
 - ▶ Mixed together
 - ▶ Diluted in different buffers
 - ▶ Assessed for particle formation and filterability

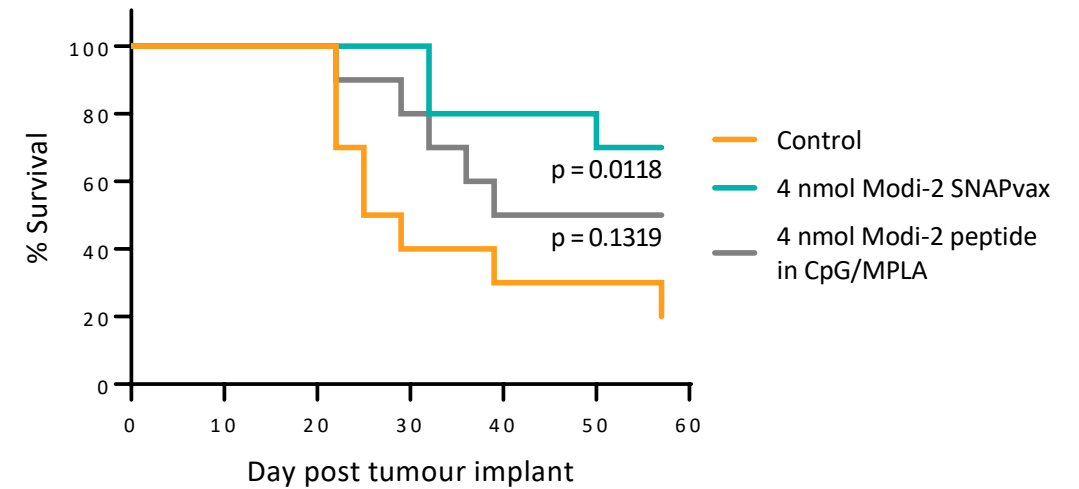
SNAPvax™ formulation

- ▶ Four peptide conjugates combined to produce mosaic particles
- ▶ Nanoparticles formed with consistent 17 nm diameter
- ▶ Buffer formulation identified for clear solution



Modi-2 SNAPvax™ particles mediate tumour therapy

- ▶ Balb/c mice injected with 4T1 tumour cells
- ▶ Tumours allowed to develop for 4 days
- ▶ Treated with Modi-2 SNAPvax™ mosaic particles or Modi-2 peptides mixed with CpG/MPLA adjuvant
- ▶ 70% of animals treated with Modi-2 SNAPvax™ particles survived



ImmunoBody®

SCIB1 – Phase 1/2 reduced recurrence and turned cancer into a chronic disease

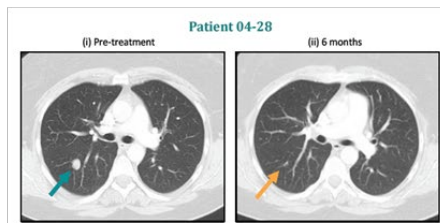
88% of patients remained disease-free for 5+ years

Two stage III/IV patients (of 15) had a measurable reduction in tumour size following treatment

Seven had stable disease for 16+ weeks

PATIENT #1

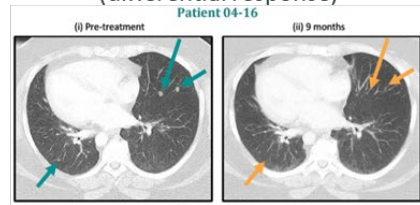
Received 8 mg and showed a marked reduction in size of detectable lung lesions



PATIENT #2

Received 4 mg and had multiple lesions decrease in size or disappear except for one lesion, which was resected

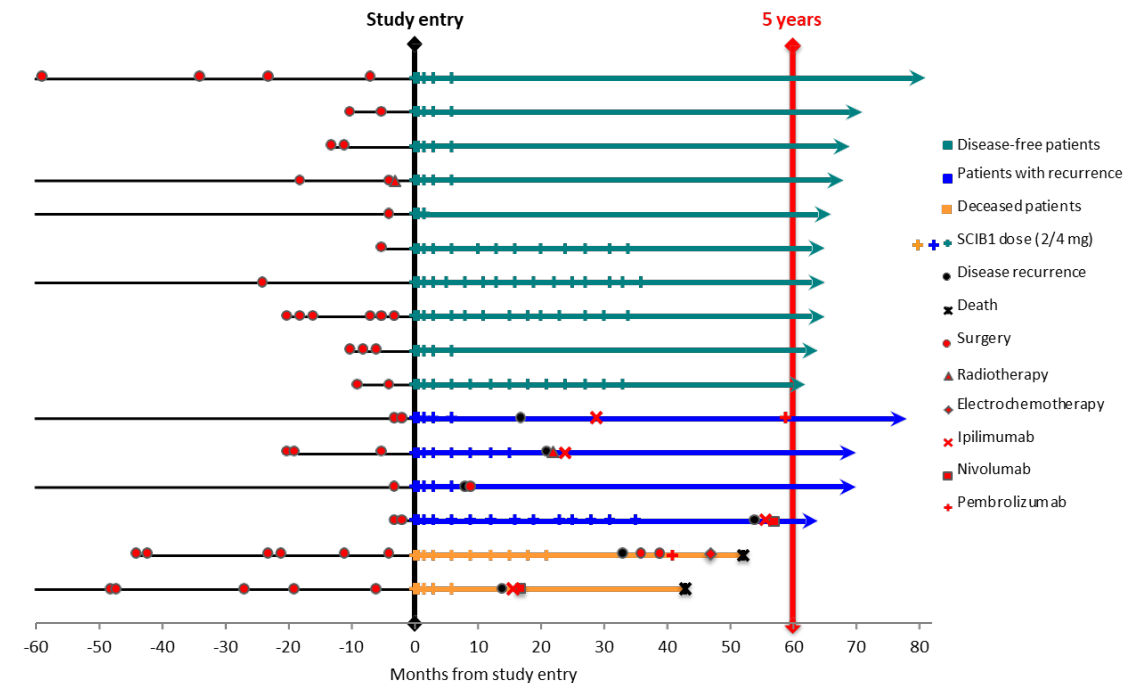
(differential response)



Patients with tumour present at study entry

14/16 patients with resected tumours were disease free after 5 years

Only four had additional treatments following recurrence



Patients without tumour present at study entry

Transition from SCIB1 to iSCIB1+ to increase potency

Needle-free delivery, improved vaccine without HLA restriction

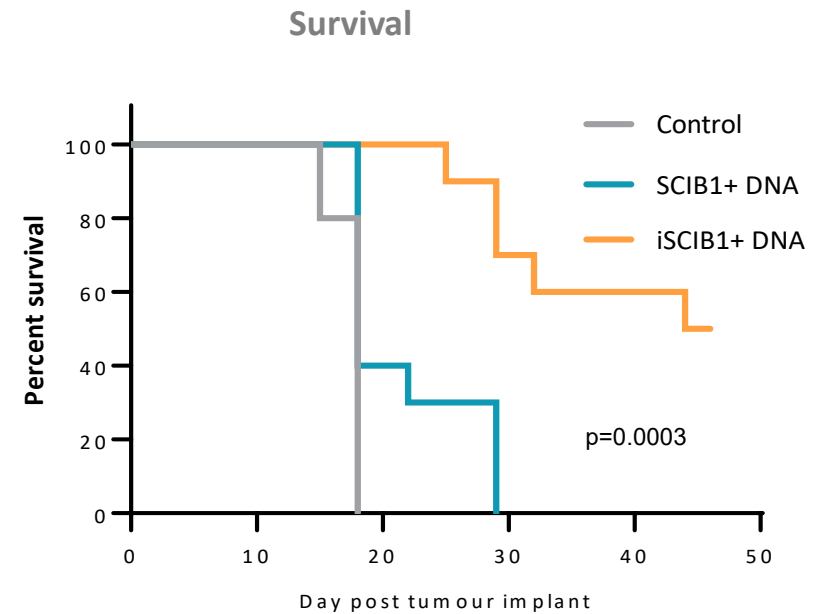
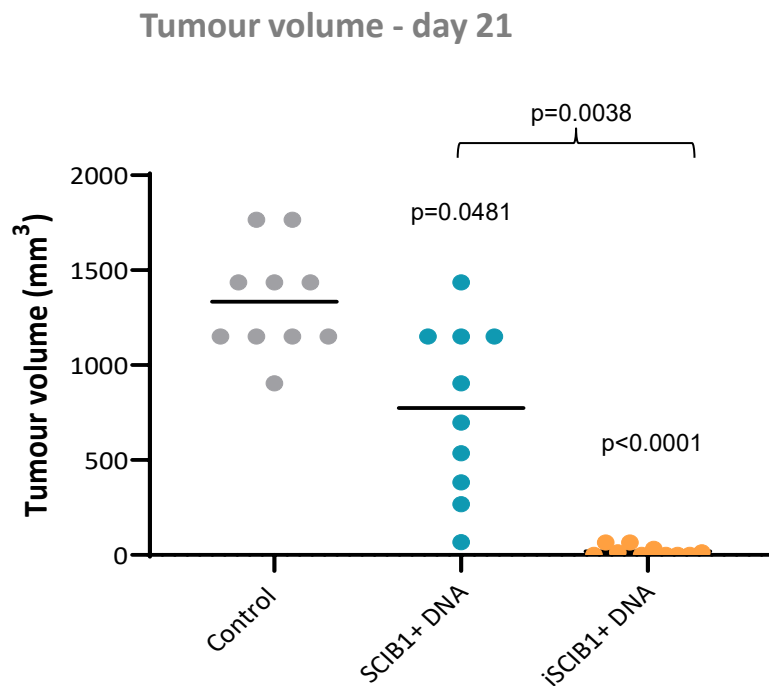
- ▶ Phase 2 SCOPE trial actively recruiting patients with metastatic melanoma receiving checkpoint inhibitor
- ▶ Transitioned from electroporation to PharmaJet needle-free delivery
- ▶ Recruitment remains challenged by HLA-A2 restriction (40% of patients)

- ▶ iSCIB1+ increases the potency of SCIB1
- ▶ iSCIB1+ includes multiple epitopes so it can be used to treat all patients
- ▶ Has AvidiMab® modification to enhance efficacy and extend patent life
- ▶ Aim to include in SCOPE trial in 2023



iSCIB1+ reduces tumour volume and increases survival compared to SCIB1+ in preclinical model

- ▶ B16 tumours established in C57Bl mice (day 1)
- ▶ iSCIB1+ or SCIB1+ (no AvidiMab®) administered on d3, d11 and d18
- ▶ 50% of iSCIB1+ animals treated survived
- ▶ Survival in treated groups statistically significant compared to control



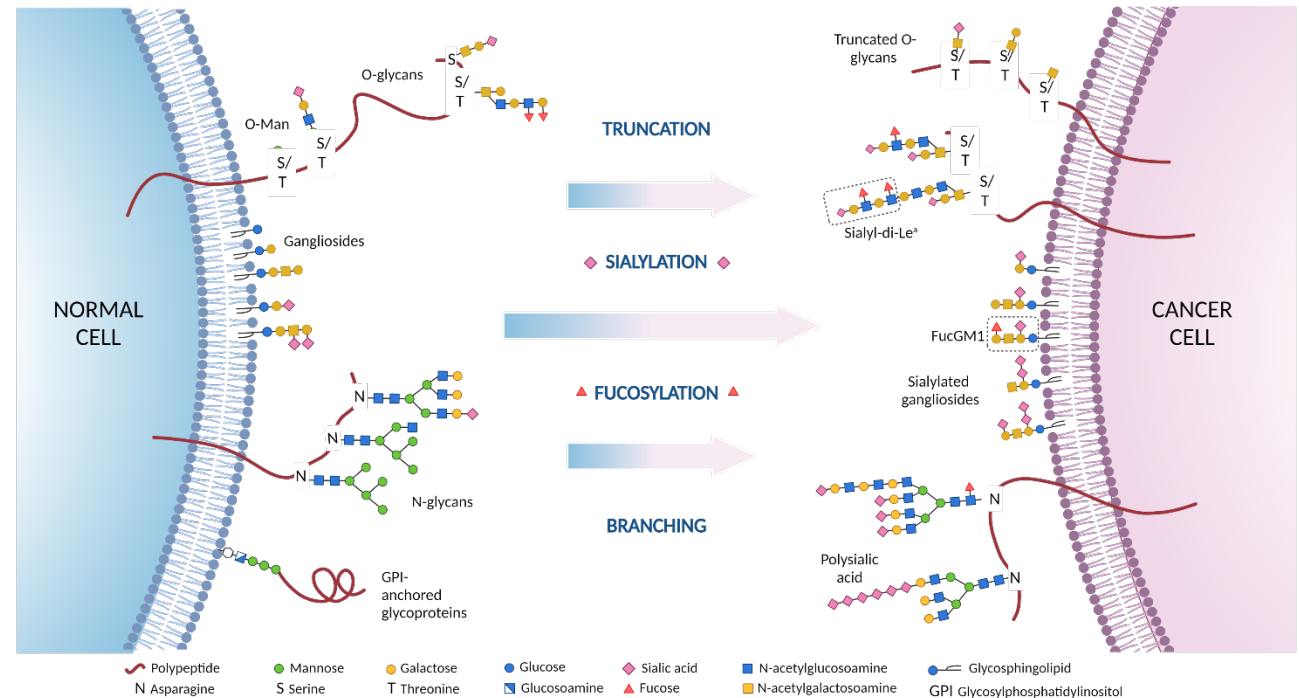
**Unique antibodies targeting
glycan modifications**



- ▶ Scancell is one of a few companies in the world able to make high affinity, humanised/human IgG anti-glycan antibodies
- ▶ Portfolio of patent protected anti-glycan antibodies with excellent specificity, binding strongly to tumours and showing restricted normal tissue expression

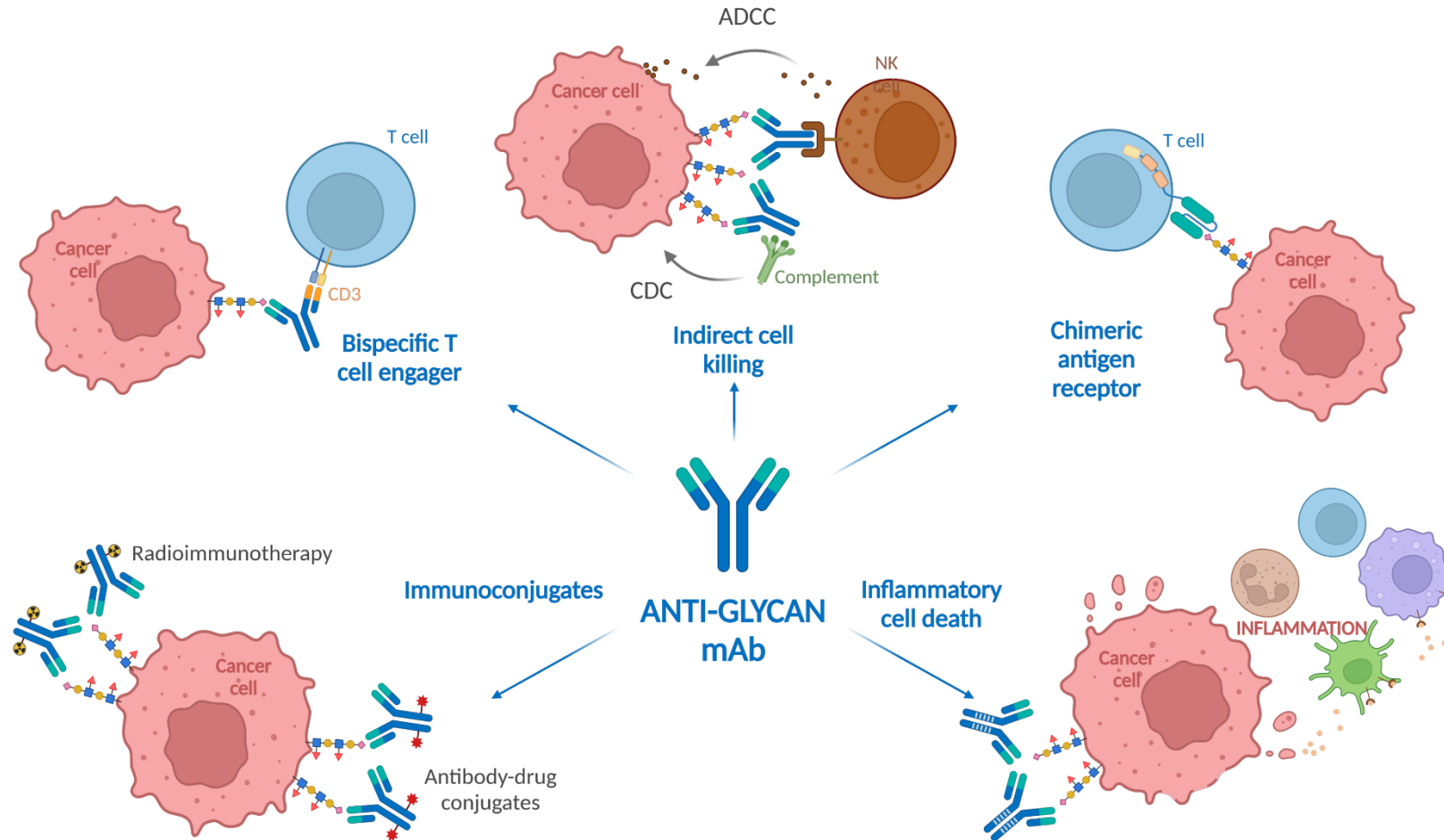
Current GlyMab[®] assets

SC129	<ul style="list-style-type: none"> • Genmab licensed asset • Sialyl-di-Lewis^a • Pancreatic cancer
SC134	<ul style="list-style-type: none"> • TCB lead target • Fucosyl GM1 • Small cell lung cancer
SC2811	<ul style="list-style-type: none"> • Stimulatory mAb target • SSEA4 • Any solid tumour
SC88	<ul style="list-style-type: none"> • Lewis^{acx} • Colorectal cancer
SC27	<ul style="list-style-type: none"> • Lewis^y • Ovarian cancer



Each antibody can be developed into multiple products

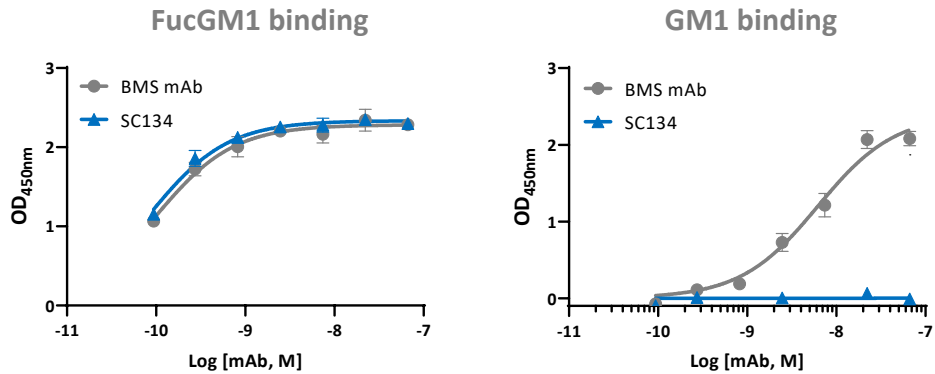
Expression of same glycan on multiple proteins and lipids



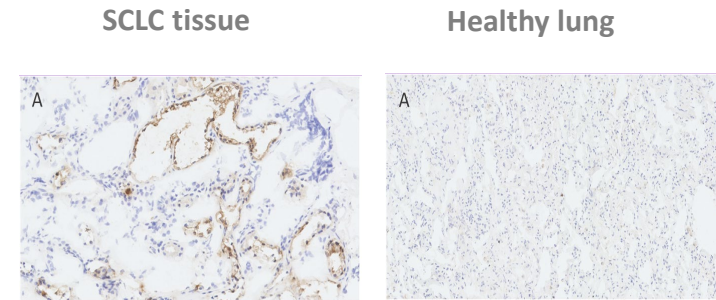
NK cell = natural killer cell; ADCC = antibody-dependent cellular cytotoxicity; CDC = complement-dependent cytotoxicity

SC134 – a highly specific antibody targeting small cell lung cancer

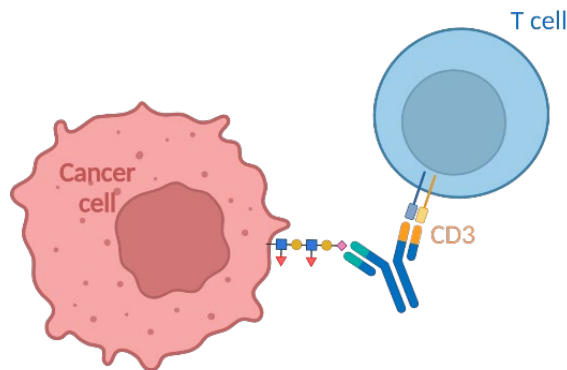
No cross reactivity with GM1 expressed on neuronal cells
SC134 compares favourably to BMS mAb



Excellent specificity – binds to SCLC but not any healthy tissue
Immunohistochemistry on frozen tissue

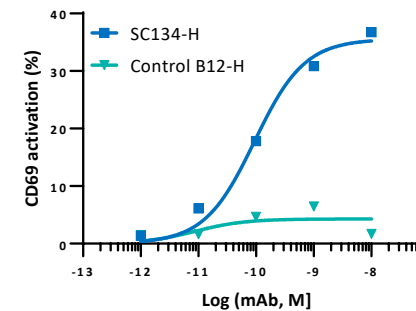


SC134 linked with scFv fragment of CD3 mAb – lead clinical candidate

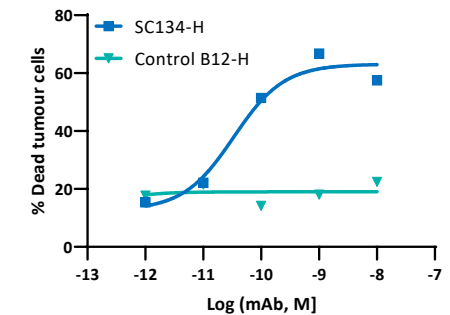


SC134-H activates T cells and kills tumour cells

Picomolar activation of T cells



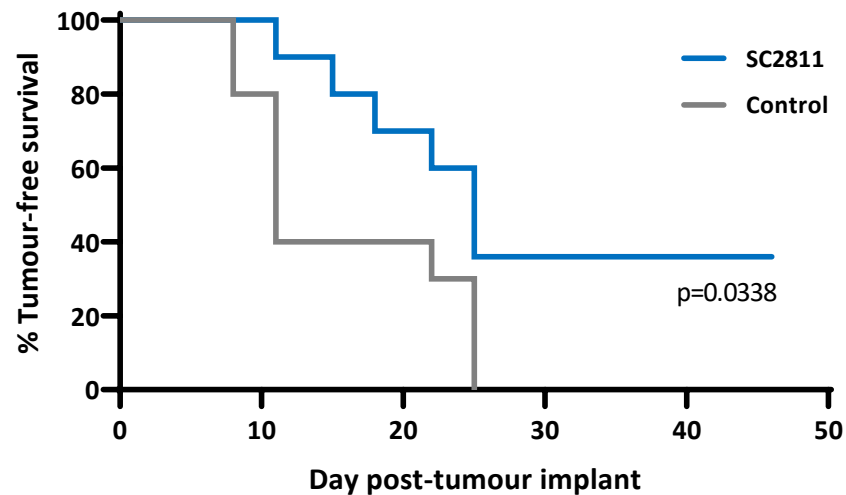
SC134-H mediates T cell tumour killing



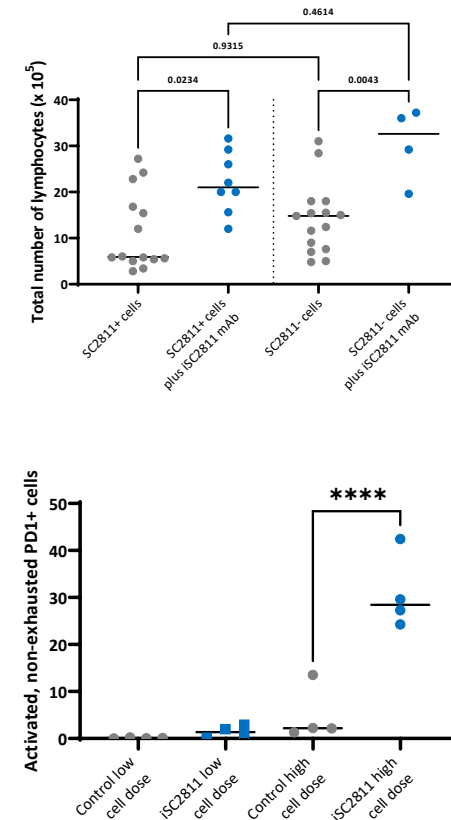
iSC2811 – costimulates TILs resulting in anti-tumour immunity and enhances T cell engraftment for CAR-T development

Ultraspecific SSEA4 mAb – lead AvidiMab® modified clinical candidate

SC2811 mediates tumour-free survival in preclinical models

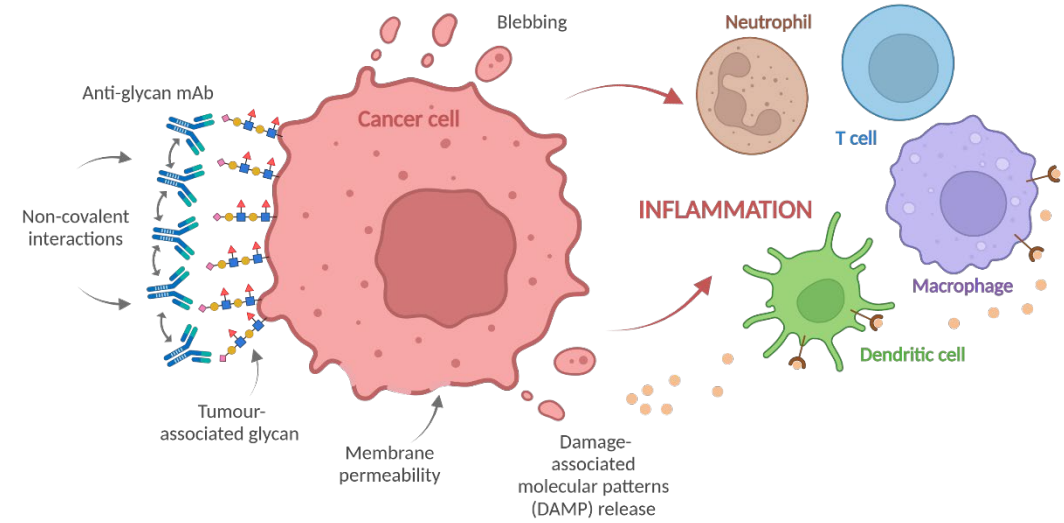


iSC2811 enhances T cell engraftment and prevents exhaustion Potential for improving CAR-T approaches

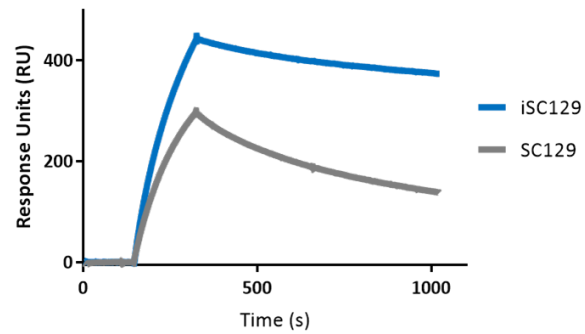


AvidiMab® – a proprietary platform for enhancing the avidity of any antibody

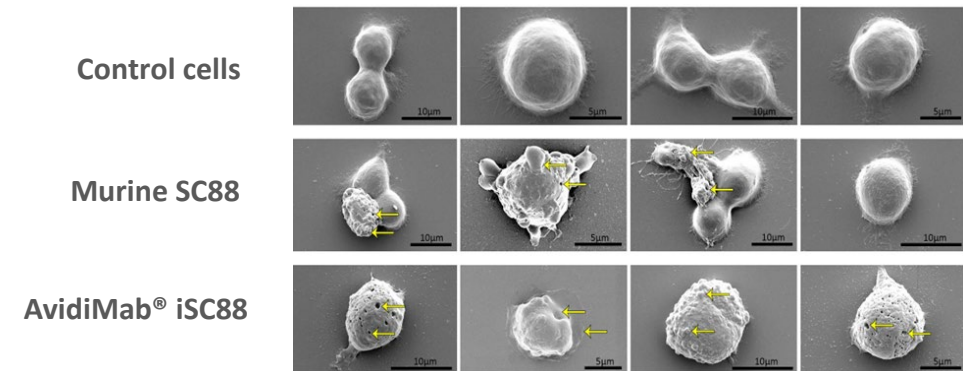
- ▶ Enhances avidity by promoting Fc-Fc interactions
- ▶ Reduces off-rate → increased affinity
- ▶ Increases direct cell-killing
- ▶ Potential to improve the therapeutic index of any monoclonal antibody
- ▶ Patent protected



AvidiMab® modification of SC129 reduces the off-rate



SC88 induces pore formation



Vankemmelbeke et al., Cancer Res., 2020 Aug 15;80(16):3399-3412

Current

- Delivered three vaccines into the clinic and an antibody deal in last 12 months

Future

- Clinical validation of vaccine assets
- Require further funding to clinically validate antibody assets

Prospects

- Multiple opportunities for further deals and products from our four platforms

Thank you

www.scancell.co.uk